

Design of Benzotriazole Coupling Reagents

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The purpose is to find a suitable route for the synthesis of benzotriazole coupling reagents, simplify the synthesis steps and reduce the synthesis cost. In this paper, the synthesis techniques of benzotriazole coupling reagent HCTV have been studied, and a better synthesis route has been found. The design of benzotriazole coupling reagents, takes dichloronitrobenzene and hydrazine hydrate as the main raw materials. After four reaction processes, such as welding, salt formation and nucleophilic substitution, HCTC is obtained. With HCTC as the lead compound, it was chemically modified with other additives to find a new design route for benzotriazole coupling reagent.

1. Introduction

At present, there are mainly two kinds of benzotriazole coupling reagents, HOBBT / DCC and HAPYU. However, the design routes of these two kinds of benzotriazole coupling reagents are poor in terms of increasing reaction rate and suppressing racemization, so it is necessary to optimize the design of benzotriazole coupling reagent.

In this paper, HCTC is used as the lead compound to modify its ammonium salt structure so as to finally synthesize 10 chemical compounds. The design of benzotriazole coupling reagent is optimized.

2. Literature review

Benzotriazole compounds are a class of efficient trio coupling agents, which can significantly reduce the common side effects such as cyclization and racemization in skin synthesis. Most of these coupling agents are non-toxic and non-corrosive, and they are stable in nature and easy to preserve. Moreover, they are of great value in the synthesis process.

Zhang and other scholars systematically studied the classification, properties and application of skin synthetic coupling reagents, and briefly introduced the research process of the benzotriazole coupling reagents. They also focused on the synthesis process of the technique of the benzotriazole coupling reagent, and determined a suitable synthetic route. The reaction takes chloro nitrobenzene and hydrated forest as starting materials, and HCTU is obtained by cyclization, acylation, salt formation and nucleophilic substitution four steps. With HCTU as the lead compound, 10 compounds were synthesized by structural modification to the salt part, of which 9 were new compounds that had not been reported in the literature. The results of the activity test showed that the new coupling reagent was close to or exceeded the HCTU activity in terms of increasing reaction rate and inhibiting the racemization, which was better than that of HOBtDCC, HAPyU and other traditional coupling agents (Zhang et al., 2016). Zang et al. used sol-gel coating technology to prepare SPME fibers by coating the metal organic frameworks UiO-67 onto the stainless steel line. The prepared fibers were used for the determination of five nitrobenzene compounds in water samples by headspace solid phase microextraction before gas chromatography. The effects of extraction temperature, extraction time, volume of sample solution, salt and desorption conditions on the extraction efficiency were optimized. The total energy and ionization cross sections of benzene, halogenated benzene, toluene, aniline and phenol in the electron scattering range are reported in a wide energy range. The multi-scattering center spherical composite optical potential method has been used to find the total elastic and inelastic cross sections (Zang et al., 2016). Sang et al. applied the complex scattering potential - ionization contribution method to estimate total ionization cross

sections from the total inelastic cross-section (Sang et al., 2016). For the purpose of most practical applications, the first theoretical calculation of the total electron ionization cross section is carried out. In comparison with the existing experimental observations for all the targets reported here, a reasonable agreement is obtained, especially for the total cross section.

Li and so on found that the new $\text{Bi}_2\text{MoO}_6 / \text{TiO}_2$ heterostructure microspheres were successfully synthesized by a simple solvothermal method. The morphology, structure and photocatalytic properties were characterized by scanning electron microscopy, transmission electron microscopy, X-ray diffraction, X-ray photoelectron spectroscopy, electrochemical impedance spectroscopy, UV visible absorption spectrum and total organic carbon analyzer, and the degradation of phenol and nitrobenzene was also characterized. The results show that the improved photocatalytic performance is mainly attributed to the reduction of electron hole pair recombination with the introduction of TiO_2 (Li et al., 2016). Spindle and others prepared 90 weight% blends of nylon-6 and 10 weight% EPDM (ethylene propylene diene monomer) rubber. Rubber was grafted with different amounts of maleic anhydride (MA) by peroxide. The initial modulus and melt viscosity of rubber were only affected by a small fraction of MA and peroxide concentration. The effects of MA concentration on the blending process and influence behavior were studied. Infrared spectroscopy and elemental analysis were used to study the interface layer. It was found that MA, which was grafted onto the rubber, reacted with nylon during mixing. Using MA grafted rubber, better dispersion can be obtained. However, the concentration of the coupling agent was grafted on the rubber in the range of 0.13 to 0.89wt%, which almost did not affect the dispersing process or the impact behavior of the blends (Spindle et al., 2017). Hybrid composites consisting of polypropylene (PP) and sisal hemp fibers were prepared by melt mixing and then pressing. Various types of chemical treatment such as alkali treatment, cyanlation, coupling agent treatment were carried out to improve the interfacial adhesion between fiber and PP substrate. The changes of fiber loading, fiber length, coupling agent concentration and treatment time with mechanical strength were studied. Thermal measurements through DSC were also studied by Mohanty and so on to confirm the discovery of mechanical data (Mohanty et al., 2016). For bonding indirect restorations, some "general" adhesives were added to the silane coupling agent to combine chemically with glass rich ceramics, claiming that a separate ceramic primer was no longer required. Through this work, Borggreve and other scholars studied the effectiveness / stability of the silane coupling function prepared by the silane and the silane coupling of the Scotchbond Universal (3MESPE). In addition, the shear bond strength of CAD-CAM composite blocks was measured before and after thermal cycling aging. Yoshihara and so on pointed out that, when the Clearfil ceramic adhesive activator just mixed with the binder, the adhesion strength was significantly higher (Yoshihara et al., 2016). Similarly, the addition of the experimental adhesive with γ -MPTS showed a significantly higher bonding strength, but only when the adhesive was applied immediately after mixing; delayed application resulted in a significant decrease in adhesive strength. FTIR and (^{13}C) nuclear magnetic resonance showed that the hydrolysis and dehydration condensation took place when the mixture of gamma -MPTS and two kinds of adhesives was mixed. After thermal cycling, only the two kinds of adhesives mixed with Clearfil vitrified bond activator can keep the bonding strength of CAD-CAM composite block stable. The silane coupling effect of the newly prepared silane containing adhesive is effective. Borggreve and so on stated that, clinically, it is recommended to use an independent silane primer or silane to blend with the binder to maintain the adhesion of glass ceramics (Borggreve et al., 2016).

To sum up, the design of benzo compound coupling reagents is still in the primary stage, especially on the design route of benzotriazole coupling agent. For the synthesis of benzotriazole coupling agent, a suitable way to simplify the synthesis process and reduce the cost of synthesis is found. The design of benzotriazole coupling agent is mainly composed of dichloronitrobenzene and hydrazine hydrate. After four reaction processes, such as welding, salt forming and nucleophilic substitution, HCTC was obtained. HCTC was used as the leading compound and chemically modified with other additives to find a new design route for benzotriazole coupling agent. Therefore, it is necessary to further explore and optimize the design of benzotriazole coupling agent.

3. Experiment

3.1 Principles of experiment

Under the conditions of strong acid, diazonium salts are produced by p-aminophenol sulfonic acid and nitrite ions. Under weak alkali conditions, this diazonium salt reacts with 8-hydroxyquinoline to form stable orange-red azo substance. The azo substance has the maximum absorption at 500 nm and the spectrophotometric method can be used to determine the chromogenic reaction of the nitrite.

3.2 Experimental instruments and experimental reagents

Instruments: 752C ultraviolet visible spectrophotometer, produced by Shanghai No. 3 Analytical Instrument Factory; precision pH test paper; sub-boiling water quartz distiller. Reagents: 1.15×10^{-2} mol/L of P-aminobenzenesulfonic acid solution; 7×10^{-3} mol/L of 8-hydroxyquinoline methanol solution; nitrite standard solution, 1.0 g / L reserve solution is prepared with sodium nitrite, and then dilute it to obtain 1×10^{-2} g/L of working solution; 0.1 mol / L of hydrochloric acid; EDTA 0.05 mol / L; and 3 mol / L of ammonia. All reagents are analytical pure or above, and water is subboiling distilled water.

3.3 Experimental methods

In a 25mL volumetric flask, add 0.4mL of 1.15×10^{-2} M p-aminobenzene sulfonic acid, 3mL of 0.1M hydrochloric acid, and a certain amount of nitrite, then mix them together. After 10 minutes, 0.6 mL of 7×10^{-3} M 8-hydroxyquinoline, 1 mL of 3 M ammonia, 0.2 mL of 0.05 EDTA are added, diluted to 25.0 mL with water and mixed. After 10 minutes, the absorbance was measured at 500nm with the reagent blank as reference. The standard solutions of 10 benzotriazole compounds are separately injected into the ion source of mass spectrometry by peristaltic pump, and then scanned in positive ion (ESI +) and negative ion (ESI -) modes to select appropriate quasi-molecular ion peaks and ionization modes. The results show that all the 10 benzotriazole compounds can obtain higher abundant M + H + quasi-molecular ion peaks under the ESI + mode. After the determination of the parent ions, the secondary mass spectrum analysis is carried out by scanning the daughter ions, and the quantitative and qualitative ions are determined by optimizing the selection of the daughter ions. Then the ion source temperature, the temperature and the flow rate of the dissolvent gas and the gas flow rate of the cone hole are optimized, so that the substance to be measured can achieve best the ionization efficiency.

4. Results and Discussions

4.1 Synthesis of HCTC

Add 4.8g (0.06mol) of o-nitroaniline, 20ml of concentrated hydrochloric acid and 40ml of water into a 250ml three-necked flask, and heat it to 70 °C. Stir it to dissolve, cool it to 0 ~ 5 °C after it is dissolved completely, and keep it at this temperature. Add 42g (0.06 mol) of sodium nitrite to a beaker with 10 ml of water, dissolve it, and then quickly add it to the above-mentioned three-necked flask for reaction. After the reaction solution is clarified, check the amount of nitrite with potassium iodide test paper, and remove it by adding an appropriate amount of urea in excess to prepare a diazonium salt solution.

4.1.1 Synthesis of intermediate A1

Add 11.8g (0.06mol) of sodium p-hydroxybenzenesulfonate, 7.0g of sodium hydroxide and 200ml of water into a 500ml beaker and stir it quickly at the reaction temperature of 0-5 °C. Then the solution of diazonium salt prepared in 2.1.1 is slowly added, and sodium hydroxide is also added in the reaction to maintain the PH value of the reaction system as 9-10. The reaction time is 2 hours. Infiltration circle method is used to test whether the diazonium salt has reacted completely. After the reaction, appropriate amount of sodium chloride and hydrochloric acid are added to separate the salt and acid. Then the intermediate A1 can be obtained after vacuum filtration and drying, with a yield of 91.8%.

Synthesis of intermediate UV1

Add 12.9g (0.04mol) of intermediate A1, 17.6g of sodium hydroxide, 320ml of water into a 500ml three-necked flask, and dissolved it at 70 °C. Then 21.6 g (0.2 mol) of thiourea dioxide (TD) are added into a three-necked flask for several times within 30 minutes, and heat it to 80°C for reaction. The end point of the reaction is detected by thin layer chromatography. After the reaction, quickly pour the reaction solution into a beaker containing ice-water mixture, and add dilute hydrochloric acid to adjust the pH value to 5.0-7.0. A small amount of sodium chloride is added and the mixture is stirred until the white particles are separated out. Then the white solid UV1 can be obtained after the mixture is vacuum filtered and dried, with a yield of 95.3%. The influence of coexisting ions is as shown in Table 1.

Table 1: Influence of coexisting ions

Ion type	Ion addition	The relative error/%
NH ₄ ⁺ /(NH ₄) ₂ SO ₄	0.028	-1.0
F ⁻ (NaF)	0.028	+1.0
Br ⁻ (KBr)	0.028	+1.1

4.1.2 Synthesis of intermediate UV1-SO₂CL

The intermediate UV1, thionyl chloride, N, and N-dimethylformamide (catalyst) with an amount of 5.8g (0.02mol), 40ml, and 0.4ml respectively are added to a 250ml three-necked flask and stirred rapidly. Then it is heated to 60°C for reaction for a period of 2 hours, then detect the reaction end point with thin layer chromatography (TLC). After the reaction, the excess thionyl chloride is distilled off under reduced pressure and recovered. The distilled substance is poured into a beaker containing ice-water mixture. Then the mixture is filtered by suction. The filter cake is washed with water until neutral. After drying, the intermediate UV1-SO₂CL can be obtained after filter cake is recrystallized from toluene.

Synthetic product UVH-1

Add the intermediate UV1-SO₂CL, potassium carbonate, acetone, and tetramethylpiperidine amine with a respective amount of 3.1g (0.01mol), 1.4g (0.01mol), 50ml, and 3.2g (0.02mol) in to a 250ml three-necked flask and stir it for reaction at room temperature. Thin-layer chromatography is used to monitor the reaction process. After the reaction, the solvent acetone is distilled off, the product is washed with dilute hydrochloric acid, the mixture is suction filtered and the filter cake is washed with water until neutral. Then the product UVH-1 can be obtained after vacuum drying.

4.2 Factors affecting the synthesis of UVH-1

In the synthesis of the intermediate UV1-SO₂CL, the thionyl chloride is the chlorination reagent and the reaction medium. Under the action of N, N-dimethylformamide as the catalyst, -SO₃H is converted into -SO₂CL. N, N-dimethylformamide is a commonly used catalyst for the conversion between such groups. The intermediate formed through the reaction of N, N-dimethylformamide with thionyl chloride is called Vilsmeier-Haack reagent, as shown in Figure 1.



Figure 1: Reaction process diagram

It is shown that the A1 reductive ring closure reaction produces intermediate UV1. ESIMS (m/z, %) 290.0 (M-NA, 100). The theoretical molecular weight of UV1 is 291.0. Through mass spectrometry analysis, the synthesized intermediate UV1 has a very strong M-H-quasi-molecular ion peak at the m/z of 290.0. It can be concluded that relative molecular weight of the intermediate UV1 is 291.0, which is consistent with the theoretical molecular weight of the intermediate UV1. It is seen from mass spectrometry that the intermediate (UV1) has been synthesized.

FTIR (ATR) / cm⁻¹: 3398.4 (OH), 1377.1, 1172.6 (SO₂-Cl). FTIR (ATR) data show that the symmetrical stretching vibration and antisymmetrical stretching vibration of -SO₂- are 1172.6cm⁻¹ and 1377.1cm⁻¹, respectively, compared with UV1, because -Cl replaces -OH on -SO₃H of UV1, and due to -Cl's strong electron absorption ability, the electron cloud density of -SO₂ decreases, and the peak position shifts to the high frequency, which is consistent with the structure of UV1-SO₂CL.

Structure analysis of product UVH-1

It can be seen from Figure 2 that 2758.4, 2830.5, 2918.3cm⁻¹ and 2996.7 cm⁻¹ are the symmetrical and antisymmetrical vibrational peaks of -CH₂- and -CH₃ on the tetramethylpiperidin amine fragment, respectively. The 3401.1cm⁻¹ is the stretching absorption peak of -OH on benzene ring, while 1162.4 and 1334.9 cm⁻¹ are the symmetrical stretching vibration and anti-symmetrical stretching vibration of -SO₂NH-. Compared to the infrared data of sulfonyl chloride, absorption of -SO₂Cl disappears in this figure, and the appearance of -SO₂NH-, -CH₃ and -CH₂-peaks indicates that the product has been synthesized.

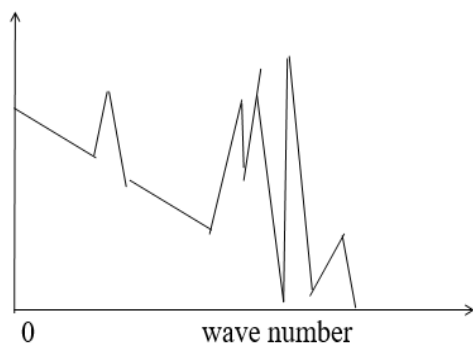


Figure 2: Transmissivity

The theoretical relative molecular weight of UVH-1 is 429.2. It can be seen from Figure 3 that the m/z of the strong quasi-molecular ion peak $(M + H)^+$ appears at 430.2, which is in accordance with the theoretical molecular weight of UVH-1. The product has been synthesized as indicated by mass spectrometry.

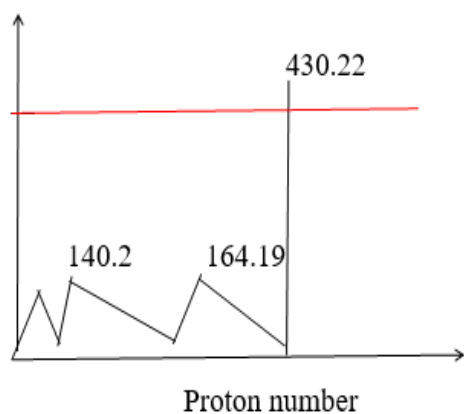


Figure 3: Relative abundance

There is a single peak at $\delta 11.61$, it is due to the fact that the nitrogen in benzotriazole and the hydrogen in the hydroxyl group form an intramolecular six-membered ring in the nuclear magnetic spectrogram of UVH-1 of Figure 4, which makes its chemical shift moves to the low shift field.

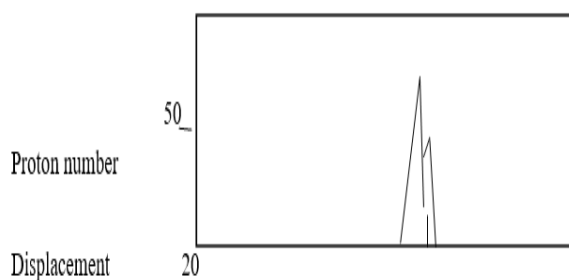


Figure 4: The chromatogram of the target compound

5. Conclusions

UVA-HALS light stabilizer UVH-1 is synthesized by introducing UV-absorbing fragment and hindered amine fragment into the same molecule through diazotization, coupling, reductive ring closure, acid chlorination and amination. The synthesized intermediates and the final products were characterized by liquid phase, mass

spectrometry, infrared spectroscopy, and nuclear magnetic hydrogen spectroscopy, which proves that their molecular structure is correct and the light stabilizer in a single molecule has both ultraviolet absorption function and free radical capture function, which has a broad application prospect.

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